



SEQUENCE LISTING

<110> Wyeth
Wolfman, Neil

<120> MODIFIED AND STABILIZED GDF PROPEPTIDES AND USES THEREOF

<130> 08702.0100-00000

<150> 10/071,499

<151> 2002-02-08

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<151> 2001-02-08

<160> 23

<170> PatentIn version 3.1

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<210> 1

<211> 375

<212> PRT

<213> Homo sapiens

<400> 1

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
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Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu Asn
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Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn Thr
35 40 45

Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys Leu
50 55 60

Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln Leu
65 70 75 80

Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val
85 90 95

Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His
100 105 110

Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe Leu
115 120 125

Met	Gln	Val	Asp	Gly	Lys	Pro	Lys	Cys	Cys	Phe	Phe	Lys	Phe	Ser	Ser	130	135	140	
Lys	Ile	Gln	Tyr	Asn	Lys	Val	Val	Lys	Ala	Gln	Leu	Trp	Ile	Tyr	Leu	145	150	155	160
Arg	Pro	Val	Glu	Thr	Pro	Thr	Thr	Val	Phe	Val	Gln	Ile	Leu	Arg	Leu	165	170	175	
Ile	Lys	Pro	Met	Lys	Asp	Gly	Thr	Arg	Tyr	Thr	Gly	Ile	Arg	Ser	Leu	180	185	190	
Lys	Leu	Asp	Met	Asn	Pro	Gly	Thr	Gly	Ile	Trp	Gln	Ser	Ile	Asp	Val	195	200	205	
Lys	Thr	Val	Leu	Gln	Asn	Trp	Leu	Lys	Gln	Pro	Glu	Ser	Asn	Leu	Gly	210	215	220	
Ile	Glu	Ile	Lys	Ala	Leu	Asp	Glu	Asn	Gly	His	Asp	Leu	Ala	Val	Thr	225	230	235	240
Phe	Pro	Gly	Pro	Gly	Glu	Asp	Gly	Leu	Asn	Pro	Phe	Leu	Glu	Val	Lys	245	250	255	
Val	Thr	Asp	Thr	Pro	Lys	Arg	Ser	Arg	Arg	Asp	Phe	Gly	Leu	Asp	Cys	260	265	270	
Asp	Glu	His	Ser	Thr	Glu	Ser	Arg	Cys	Cys	Arg	Tyr	Pro	Leu	Thr	Val	275	280	285	
Asp	Phe	Glu	Ala	Phe	Gly	Trp	Asp	Trp	Ile	Ile	Ala	Pro	Lys	Arg	Tyr	290	295	300	
Lys	Ala	Asn	Tyr	Cys	Ser	Gly	Glu	Cys	Glu	Phe	Val	Phe	Leu	Gln	Lys	305	310	315	320
Tyr	Pro	His	Thr	His	Leu	Val	His	Gln	Ala	Asn	Pro	Arg	Gly	Ser	Ala	325	330	335	
Gly	Pro	Cys	Cys	Thr	Pro	Thr	Lys	Met	Ser	Pro	Ile	Asn	Met	Leu	Tyr	340	345	350	

Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ala Met Val
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Val Asp Arg Cys Gly Cys Ser
 370 375

<210> 2
 <211> 1125
 <212> DNA
 <213> Homo sapiens

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 gcatgtactt ggagacaaaa cactaaatct tcaagaatag aagccattaa gatacaaatc
 180
 ctacgtaaac ttcgtctgga aacagctcct aacatcagca aagatgttat aagacaactt
 240
 ttacccaaag ctctccact ccgggaactg attgatcagt atgatgtcca gagggatgac
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 agcagcgatg gctcttttga agatgacgat tatcacgcta caacggaaac aatcattacc
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 aaatttagct ctaaaataca atacaataaa gtagtaaagg cccaactatg gatatatattg
 480
 agacccgtcg agactcctac aacagtgttt gtgcaaatcc tgagactcat caaacctatg
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 ggtatttggc agagcattga tgtgaagaca gtgttgcaaa attgggtcaa acaacctgaa
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 720
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tgctgtcggtt accctctaac tgtggatttt gaagcttttg gatgggattg gattatcgct
900

cctaaaagat ataaggccaa ttactgctct ggagagtgtg aatttgtatt ttacaaaaa
960

tatcctcata ctcatctggt acaccaagca aaccccagag gttcagcagg cccttgctgt
1020

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1080

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<210> 3
<211> 109
<212> PRT
<213> Homo sapiens

<400> 3

Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg Cys Cys
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Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
20 25 30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu
35 40 45

Phe Val Phe Leu Gln Lys Tyr Pro His Thr His Leu Val His Gln Ala
50 55 60

Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly
85 90 95

Lys Ile Pro Ala Met Val Val Asp Arg Cys Gly Cys Ser
100 105

<210> 4
<211> 327
<212> DNA
<213> Homo sapiens

<400> 4

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actgtggatt ttgaagcttt tggatgggat tggattatcg ctcctaaaag atataaggcc
120

aattactgct ctggagagtg tgaatttgta tttttacaaa aatatacctca tactcatctg
180

gtacaccaag caaaccccag aggttcagca ggcccttgct gtactccac aaagatgtct
240

ccaattaata tgctatattt taatggcaaa gaacaaataa tatatgggaa aattccagcg
300

atggtagtag accgctgtgg gtgctca
327

<210> 5
<211> 243
<212> PRT
<213> Homo sapiens

<400> 5

Asn Glu Asn Ser Glu Gln Lys Glu Asn Val Glu Lys Glu Gly Leu Cys
1 5 10 15

Asn Ala Cys Thr Trp Arg Gln Asn Thr Lys Ser Ser Arg Ile Glu Ala
20 25 30

Ile Lys Ile Gln Ile Leu Ser Lys Leu Arg Leu Glu Thr Ala Pro Asn
35 40 45

Ile Ser Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu
50 55 60

Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp
65 70 75 80

Gly Ser Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile
85 90 95

Thr Met Pro Thr Glu Ser Asp Phe Leu Met Gln Val Asp Gly Lys Pro
100 105 110

Lys Cys Cys Phe Phe Lys Phe Ser Ser Lys Ile Gln Tyr Asn Lys Val
115 120 125

Val Lys Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Glu Thr Pro Thr
 130 135 140

Thr Val Phe Val Gln Ile Leu Arg Leu Ile Lys Pro Met Lys Asp Gly
 145 150 155 160

Thr Arg Tyr Thr Gly Ile Arg Ser Leu Lys Leu Asp Met Asn Pro Gly
 165 170 175

Thr Gly Ile Trp Gln Ser Ile Asp Val Lys Thr Val Leu Gln Asn Trp
 180 185 190

Leu Lys Gln Pro Glu Ser Asn Leu Gly Ile Glu Ile Lys Ala Leu Asp
 195 200 205

Glu Asn Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro Gly Glu Asp
 210 215 220

Gly Leu Asn Pro Phe Leu Glu Val Lys Val Thr Asp Thr Pro Lys Arg
 225 230 235 240

Ser Arg Arg

<210> 6
 <211> 729
 <212> DNA
 <213> Homo sapiens

<400> 6
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tggagacaaa aactaaatc ttcaagaata gaagccatta agatacaaat cctcagtaaa
 120

cttcgtctgg aaacagctcc taacatcagc aaagatgtta taagacaact ttaccctaaa
 180

gctcctccac tccgggaact gattgatcag tatgatgtcc agagggatga cagcagcgat
 240

ggctctttgg aagatgacga ttatcacgct acaacggaaa caatcattac catgcctaca
 300

gagtcctgatt ttctaatagca agtggatgga aaacccaaat gttgcttctt taaatttagc
 360

tctaaaatac aatacaataa agtagtaaag gcccaactat ggatatattt gagaccgctc
420

gagactccta caacagtgtt tgtgcaaatac ctgagactca tcaaacttat gaaagacggt
480

acaaggtata ctggaatccg atctctgaaa cttgacatga acccaggcac tggatatttg
540

cagagcattg atgtgaagac agtgttgcaa aattggctca aacaacctga atccaactta
600

ggcattgaaa taaaagcttt agatgagaat ggcatgatc ttgctgtaac cttcccagga
660

ccaggagaag atgggctgaa tccgttttta gaggtcaagg taacagacac accaaaaaga
720

tccagaagg
729

<210> 7
<211> 407
<212> PRT
<213> Homo sapiens

<400> 7

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala Ala Glu Gly Pro Ala Ala Ala Ala
20 25 30

Ala Ala Ala Ala Ala Ala Ala Ala Ala Gly Val Gly Gly Glu Arg Ser
35 40 45

Ser Arg Pro Ala Pro Ser Val Ala Pro Glu Pro Asp Gly Cys Pro Val
50 55 60

Cys Val Trp Arg Gln His Ser Arg Glu Leu Arg Leu Glu Ser Ile Lys
65 70 75 80

Ser Gln Ile Leu Ser Lys Leu Arg Leu Lys Glu Ala Pro Asn Ile Ser
85 90 95

Arg Glu Val Val Lys Gln Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln
100 105 110

Ile Leu Asp Leu His Asp Phe Gln Gly Asp Ala Leu Gln Pro Glu Asp
 115 120 125

Phe Leu Glu Glu Asp Glu Tyr His Ala Thr Thr Glu Thr Val Ile Ser
 130 135 140

Met Ala Gln Glu Thr Asp Pro Ala Val Gln Thr Asp Gly Ser Pro Leu
 145 150 155 160

Cys Cys His Phe His Phe Ser Pro Lys Val Met Phe Thr Lys Val Leu
 165 170 175

Lys Ala Gln Leu Trp Val Tyr Leu Arg Pro Val Pro Arg Pro Ala Thr
 180 185 190

Val Tyr Leu Gln Ile Leu Arg Leu Lys Pro Leu Thr Gly Glu Gly Thr
 195 200 205

Ala Gly Gly Gly Gly Gly Gly Arg Arg His Ile Arg Ile Arg Ser Leu
 210 215 220

Lys Ile Glu Leu His Ser Arg Ser Gly His Trp Gln Ser Ile Asp Phe
 225 230 235 240

Lys Gln Val Leu His Ser Trp Phe Arg Gln Pro Gln Ser Asn Trp Gly
 245 250 255

Ile Glu Ile Asn Ala Phe Asp Pro Ser Gly Thr Asp Leu Ala Val Thr
 260 265 270

Ser Leu Gly Pro Gly Ala Glu Gly Leu His Pro Phe Met Glu Leu Arg
 275 280 285

Val Leu Glu Asn Thr Lys Arg Ser Arg Arg Asn Leu Gly Leu Asp Cys
 290 295 300

Asp Glu His Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val
 305 310 315 320

Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr
 325 330 335

Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu Tyr Met Phe Met Gln Lys
 340 345 350

Tyr Pro His Thr His Leu Val Gln Gln Ala Asn Pro Arg Gly Ser Ala
 355 360 365

Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr
 370 375 380

Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly Lys Ile Pro Gly Met Val
 385 390 395 400

Val Asp Arg Cys Gly Cys Ser
 405

<210> 8
 <211> 1221
 <212> DNA
 <213> Homo sapiens

<400> 8
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 120

gcgggggtcg ggggggagcg ctccagccgg ccagccccgt ccgtggcgcc cgagccggac
 180

ggctgccccg tgtgcgtttg gcggcagcac agccgcgagc tgcgcctaga gagcatcaag
 240

tcgcagatct tgagcaaact gcggctcaag gaggcgcca acatcagccg cgaggtggtg
 300

aagcagctgc tgcccaaggc gccgccgctg cagcagatcc tggacctaca cgacttccag
 360

ggcgacgcgc tgcagcccga ggacttcctg gaggaggacg agtaccacgc caccaccgag
 420

accgtcatta gcatggccca ggagacggac ccagcagtac agacagatgg cagccctctc
 480

tgctgccatt ttcaattcag cccaagggtg atgttcacaa aggtactgaa ggcccagctg
 540

tgggtgtacc tacggcctgt accccgcca gccacagtct acctgcagat cttgcgacta
 600

aaacccctaa ctggggaagg gaccgcaggg ggagggggcg gaggccggcg tcacatccgt
660

atccgctcac tgaagattga gctgcactca cgctcaggcc attggcagag catcgacttc
720

aagcaagtgc tacacagctg gttccgccag ccacagagca actggggcat cgagatcaac
780

gcctttgatc ccagtggcac agacctggct gtcacctccc tggggccggg agccgagggg
840

ctgcatccat tcatggagct tcgagtccca gagaacacaa aacgttcccg gcggaacctg
900

ggtctggact gcgacgagca ctcaagcgag tcccgtgct gccgatatcc cctcacagtg
960

gactttgagg ctttcggctg ggactggatc atcgcaccta agcgctacaa ggccaactac
1020

tgctccggcc agtgcgagta catgttcatg caaaaatata cgcataccca tttggtgcag
1080

caggccaatc caagaggctc tgctggggccc tgttgtaccc ccaccaagat gtccccaatc
1140

aacatgctct acttcaatga caagcagcag attatctacg gcaagatccc tggcatgggtg
1200

gtggatcgct gtggctgctc t
1221

<210> 9
<211> 109
<212> PRT
<213> Homo sapiens

<400> 9

Asn Leu Gly Leu Asp Cys Asp Glu His Ser Ser Glu Ser Arg Cys Cys
1 5 10 15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
20 25 30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu
35 40 45

Tyr Met Phe Met Gln Lys Tyr Pro His Thr His Leu Val Gln Gln Ala
50 55 60

Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly
85 90 95

Lys Ile Pro Gly Met Val Val Asp Arg Cys Gly Cys Ser
100 105

<210> 10
<211> 327
<212> DNA
<213> Homo sapiens

<400> 10
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acagtggact ttgaggcttt cggctgggac tggatcatcg cacctaagcg ctacaaggcc
120

aactactgct cgggccagtg cgagtacatg ttcatgcaaa aatatccgca taccatttg
180

gtgcagcagg ccaatccaag aggctctgct gggccctggt gtacccccac caagatgtcc
240

ccaatcaaca tgctctactt caatgacaag cagcagatta tctacggcaa gatccctggc
300

atggtggtgg atcgctgtgg ctgctct
327

<210> 11
<211> 274
<212> PRT
<213> Homo sapiens

<400> 11

Ala Glu Gly Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala
1 5 10 15

Ala Gly Val Gly Gly Glu Arg Ser Ser Arg Pro Ala Pro Ser Val Ala
20 25 30

Pro Glu Pro Asp Gly Cys Pro Val Cys Val Trp Arg Gln His Ser Arg
35 40 45

Glu Leu Arg Leu Glu Ser Ile Lys Ser Gln Ile Leu Ser Lys Leu Arg
 50 55 60

Leu Lys Glu Ala Pro Asn Ile Ser Arg Glu Val Val Lys Gln Leu Leu
 65 70 75 80

Pro Lys Ala Pro Pro Leu Gln Gln Ile Leu Asp Leu His Asp Phe Gln
 85 90 95

Gly Asp Ala Leu Gln Pro Glu Asp Phe Leu Glu Glu Asp Glu Tyr His
 100 105 110

Ala Thr Thr Glu Thr Val Ile Ser Met Ala Gln Glu Thr Asp Pro Ala
 115 120 125

Val Gln Thr Asp Gly Ser Pro Leu Cys Cys His Phe His Phe Ser Pro
 130 135 140

Lys Val Met Phe Thr Lys Val Leu Lys Ala Gln Leu Trp Val Tyr Leu
 145 150 155 160

Arg Pro Val Pro Arg Pro Ala Thr Val Tyr Leu Gln Ile Leu Arg Leu
 165 170 175

Lys Pro Leu Thr Gly Glu Gly Thr Ala Gly Gly Gly Gly Gly Gly Arg
 180 185 190

Arg His Ile Arg Ile Arg Ser Leu Lys Ile Glu Leu His Ser Arg Ser
 195 200 205

Gly His Trp Gln Ser Ile Asp Phe Lys Gln Val Leu His Ser Trp Phe
 210 215 220

Arg Gln Pro Gln Ser Asn Trp Gly Ile Glu Ile Asn Ala Phe Asp Pro
 225 230 235 240

Ser Gly Thr Asp Leu Ala Val Thr Ser Leu Gly Pro Gly Ala Glu Gly
 245 250 255

Leu His Pro Phe Met Glu Leu Arg Val Leu Glu Asn Thr Lys Arg Ser
 260 265 270

Arg Arg

<210> 12
<211> 822
<212> DNA
<213> Homo sapiens

<400> 12
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ggggagcgct ccagccggcc agccccgtcc gtggcgcccg agccggacgg ctgccccgtg
120
tgcgtttggc ggcagcacag ccgcgagctg cgccatagaga gcatcaagtc gcagatcttg
180
agcaaaactgc ggctcaagga ggcgcccac atcagccgcg aggtggtgaa gcagctgctg
240
cccaaggcgc cgccgctgca gcagatcctg gacctacacg acttcaggcg cgacgcgctg
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cagcccaggg acttcctgga ggaggacgag taccacgcca ccaccgagac cgtcattagc
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420
cattcagcc ccaaggtgat gttcaciaaag gtactgaagg ccagctgtg ggtgtaccta
480
cggcctgtac cccgcccagc cacagtctac ctgcagatct tgcgactaaa acccctaact
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aagattgagc tgcactcacg ctcaggccat tggcagagca tcgacttcaa gcaagtgcta
660
cacagctggg tccgccagcc acagagcaac tggggcatcg agatcaacgc ctttgatccc
720
agtggcacag acctggctgt cacctocctg gggccgggag ccgaggggct gcatccattc
780
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822

<210> 13
<211> 23
<212> PRT
<213> Homo sapiens

<400> 13

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1 5 10 15

Val Ala Gly Pro Val Asp Leu
20

<210> 14

<211> 24

<212> PRT

<213> Homo sapiens

<400> 14

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala
20

<210> 15

<211> 232

<212> PRT

<213> Homo sapiens

<400> 15

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
130 135 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145 150 155 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 16
<211> 227
<212> PRT
<213> Homo sapiens

<400> 16

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Leu Gly
1 5 10 15

Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 17
<211> 4
<212> PRT
<213> Homo sapiens

<400> 17

Gly Ser Gly Ser
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<210> 18
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 <212> PRT
 <213> Human

<400> 18

Arg Ser Arg Arg
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<210> 19
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 <212> PRT
 <213> Human

<400> 19

Ala Glu Gly Pro Ala Ala Ala
 1 5

<210> 20
 <211> 498
 <212> PRT
 <213> chimera

<400> 20

Met Met Gln Lys Leu Gln Met Tyr Val Tyr Ile Tyr Leu Phe Met Leu
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 20 25 30

Asn Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Ala Trp Arg Gln Asn
 35 40 45

Thr Arg Tyr Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys
 50 55 60

Leu Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Ala Ile Arg Gln
 65 70 75 80

Leu Leu Pro Arg Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp
 85 90 95

Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr
 100 105 110

His Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe
 115 120 125

Leu Met Gln Ala Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser
 130 135 140

Ser Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr
 145 150 155 160

Leu Arg Pro Val Lys Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg
 165 170 175

Leu Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser
 180 185 190

Leu Lys Leu Asp Met Ser Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp
 195 200 205

Val Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu
 210 215 220

Gly Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val
 225 230 235 240

Thr Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val
 245 250 255

Lys Val Thr Asp Thr Pro Lys Arg Ser Glu Pro Arg Gly Pro Thr Ile
 260 265 270

Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Glu Gly Gly
 275 280 285

Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile
 290 295 300

Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp
 305 310 315 320

Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His
 325 330 335

Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg
 340 345 350

Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys
 355 360 365

Ala Phe Ala Cys Ala Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu
 370 375 380

Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr
 385 390 395 400

Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu
 405 410 415

Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp
 420 425 430

Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val
 435 440 445

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu
 450 455 460

Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His
 465 470 475 480

Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro
 485 490 495

Gly Lys

<210> 21
 <211> 496
 <212> PRT
 <213> chimera

<400> 21

Met Met Gln Lys Leu Gln Phe Ile Tyr Val Tyr Ile Tyr Leu Phe Asn
 1 5 10 15

Leu Ile Ala Ala Gly Pro Val Asp Leu Asn Asn Ile Glu Gly Ser Glu
 20 25 30

Arg Glu Glu Asn Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Ala Trp
 35 40 45

Arg Gln Asn Thr Arg Tyr Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile
 50 55 60

Leu Ser Lys Leu Arg Leu Glu Thr Ala Pro Ile Asn Ile Ser Lys Asp
 65 70 75 80

Ala Ile Arg Gln Leu Leu Pro Arg Ala Pro Pro Leu Arg Glu Leu Ile
 85 90 95

Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu
 100 105 110

Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr
 115 120 125

Glu Ser Asp Phe Leu Met Gln Ala Asp Gly Lys Pro Lys Cys Cys Phe
 130 135 140

Phe Lys Phe Ser Ser Lys Ile Gln Tyr Asn Asn Asn Lys Val Val Lys
 145 150 155 160

Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Lys Thr Pro Thr Thr Val
 165 170 175

Phe Val Gln Ile Leu Arg Leu Ile Lys Pro Met Lys Asp Gly Thr Arg
 180 185 190

Tyr Thr Gly Ile Arg Ser Leu Lys Leu Asp Met Ser Pro Gly Thr Gly
 195 200 205

Ile Trp Gln Ser Ile Asp Val Lys Thr Val Leu Gln Asn Trp Leu Lys
 210 215 220

Gln Pro Glu Ser Asn Leu Gly Ile Glu Ile Lys Ala Leu Asp Glu Asn
 225 230 235 240

Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro Gly Glu Asp Gly Leu
 245 250 255

Asn Pro Phe Leu Glu Val Lys Val Thr Asp Thr Pro Lys Arg Ser Gly
 260 265 270

Ser Gly Ser Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys
 275 280 285

Lys Cys Pro Ala Pro Asn Leu Glu Gly Gly Pro Ser Val Phe Ile Phe
 290 295 300

Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile Val
 305 310 315 320

Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln Ile
 325 330 335

Ser Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
 340 345 350

Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met
 355 360 365

Ser Gly Lys Ala Phe Ala Cys Ala Val Asn Asn Lys Asp Leu Pro Ala
 370 375 380

Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
 385 390 395 400

Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
 405 410 415

Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
 420 425 430

Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
 435 440 445

Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
 450 455 460

Arg Val Glu Lys Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly
 465 470 475 480

Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
485 490 495

<210> 22
<211> 497
<212> PRT
<213> chimera

<400> 22

Met Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu
1 5 10 15

Ile Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu
20 25 30

Asn Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn
35 40 45

Thr Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys
50 55 60

Leu Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln
65 70 75 80

Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp
85 90 95

Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr
100 105 110

His Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe
115 120 125

Leu Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser
130 135 140

Ser Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr
145 150 155 160

Leu Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg
165 170 175

Leu Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser
180 185 190

Leu Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp
 195 200 205

Val Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu
 210 215 220

Gly Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val
 225 230 235 240

Thr Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val
 245 250 255

Lys Val Thr Asp Thr Pro Lys Arg Ser Glu Pro Lys Ser Cys Asp Lys
 260 265 270

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 275 280 285

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 290 295 300

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 305 310 315 320

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 325 330 335

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 340 345 350

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 355 360 365

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 370 375 380

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 385 390 395 400

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
 405 410 415

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
420 425 430

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
435 440 445

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
450 455 460

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
465 470 475 480

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
485 490 495

Lys

<210> 23
<211> 491
<212> PRT
<213> chimera

<400> 23

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1 5 10 15

Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu Asn
20 25 30

Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn Thr
35 40 45

Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys Leu
50 55 60

Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln Leu
65 70 75 80

Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val
85 90 95

Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His
100 105 110

Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe Leu
115 120 125

Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser Ser
130 135 140

Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr Leu
145 150 155 160

Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg Leu
165 170 175

Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser Leu
180 185 190

Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val
195 200 205

Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly
210 215 220

Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr
225 230 235 240

Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys
245 250 255

Val Thr Asp Thr Pro Lys Arg Ser Asp Lys Thr His Thr Cys Pro Pro
260 265 270

Cys Pro Ala Pro Glu Ala Leu Gly Ala Pro Ser Val Phe Leu Phe Pro
275 280 285

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
290 295 300

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
305 310 315 320

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
325 330 335

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
 340 345 350

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
 355 360 365

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
 370 375 380

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
 385 390 395 400

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
 405 410 415

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
 420 425 430

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
 435 440 445

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
 450 455 460

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
 465 470 475 480

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 485 490